Tetrahedron Letters No. 47, pp 4581 - 4582. 0040-4039/79/1115-4581$02.00/0

POLYETHYLENE GLYCOLS AS HOST SOLVENTS: APPLICATIONS TO ORGANIC SYNTHESIS[1]

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Summary Polyethylene glycols (PEG) are fair solvents for inorganic salts and organic substrates; their use in some organic reactions is described.

Acceleration of bimolecular reactions can be achieved using polar protic and dipolar aprotic solvents, which make possible the mutual dissolution of salts and organic substrates[2]. Polyethylene glycols (PEG) of general formula $HO(CH_2-CH_2O)_nH$, can be regarded as protic solvents with aprotic sites of binding constituted by some monomeric units (CH_2-CH_2O). Surprisingly, applications to organic synthesis of PEG have not been investigated although low molecular weight PEG ($\bar{M}$ between 200 and 600) at ambient and higher temperatures exhibit a viscosity which is compatible with all general laboratory operations. Additionally, PEG seem to offer advantages such as low cost, low vapour pressure and ready availability. Use of PEG as solvents was suggested by the high solubility of some salts in PEG 400[3] (Table 1) and most of organic substrates as well.

Table 1: Solubility of salts in PEG 400 at 28°[a]

SALT	CH_3COOK	KI	KNO_3	KCN	$K_2Cr_2O_7$
SOLUBILITY (g/100g PEG)	17	35	11	1.6	4
MOLALITY	1.8	2.1	1.1	0.25	0.16

a. Solubility in DMSO at 28° (g/100 g solvent): KOAc 0.01, KI 40, KNO_3 10, KCN 0.8, $K_2Cr_2O_7$ 10.

We have therefore studied preliminary applications of PEG 400 as solvent to organic synthesis; the results are summarized in Table 2.

In a typical procedure, to a solution of the salt in PEG 400 at concentrations reported in Table 1, the organic substrates (10-50 mmoles, stoichiometric amount) are added and the solution stirred at temperature and time indicated in Table 2. The work-up can be performed in different ways, since PEG are soluble in water to a large extent and insoluble in alkanes. Therefore, products can be recovered either by addition of water, followed by extraction with solvents, or by direct extraction with pentane. For highly and medium volatile compounds a direct distillation from very low volatile PEG allows the isolation of the products with excellent recovery.

Concerning the reactions tested, oxidation of benzyl bromide with $K_2Cr_2O_7$ in PEG is similar to the reaction of sodium chromate in HMPA and crown ethers on the same substrates[4]. In our case, along with benzaldehyde as main product (85%), also 10% of benzylalcohol was isolated. Formation of benzylalcohol can be explained by hydrolysis of the intermediate chromate ester by trace of water present in the medium[5]. Reduction by means of $NaBH_4$ in PEG proceeds smoothly and efficiently in contrast with the slow reaction of $NaBH_4$ in THF in the presence of ethers of polyethylene glycols[6].

Table 2: Reactions in PEG 400 on preparative scale

SALT	SUBSTRATE	PRODUCT[a]	TIME (h)	YIELDS[b] (%)	T (°C)
$K_2Cr_2O_7$	$C_6H_5CH_2Br$	C_6H_5CHO	2	85	110
CH_3COOK	$C_{10}H_{21}Br$	$C_{10}H_{21}OAc$	0.5	92	110
	C_4H_9Br	C_4H_9OAc[c]	0.5	90	110
KCN	$C_8H_{17}Br$	$C_8H_{17}CN$	3	94	110
	C_4H_9Br	C_4H_9CN[c]	3	90	110
KI	C_4H_9Br	C_4H_9I[c]	0.5	88	110
C_6H_5OK	$C_8H_{17}Br$	$C_8H_{17}OC_6H_5$	0.5	94	110
$NaBH_4$	$CH_3COC_6H_{13}$	$CH_3CHOHC_6H_{13}$	2	90	25

a. Products were identical to authentic material, as ascertained by I.R., ^{1}H-N.M.R. as well as g.l.c. and t.l.c. analysis.
b. Isolated yields.
c. Distilled directely from the medium of reaction.

On the light of recent reports based on ^{1}H-N.M.R. studies of complexes of PEG with alkaline and alkaline earth cations in protic and aprotic solvents[7], PEG as solvents can be expected to be able to complex cations and bring into solution relatively separated anions[8]. From these considerations, a definition of PEG as "host" solvents is here proposed.

Acknowledgement: We thank Professor A.Fiecchi for many helpful discussions.

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(Received in UK 12 September 1979)